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Fabrication of an endoneurium using engineered neural tissue within a peripheral nerve repair conduit

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Fabrication of an Endoneurium using Engineered Neural Tissue within a Peripheral Nerve Repair Conduit

Peripheral nerve injury as a result of trauma affects approximately 1 million people in Europe and America annually. The current clinical gold standard treatment for repairing long gaps is the nerve autograft, in which only ~50% of cases result in satisfactory functional recovery. Tissue-engineered cellular bridging devices for peripheral nerve repair could provide an attractive alternative to autografts. Sheets of engineered neural tissue (EngNT), which is formed from columns of Schwann cells within a 3D aligned collagen matrix, can promote directed neurite outgrowth *in vitro*. These sheets of EngNT can be arranged to form the 'endoneurium' of a peripheral nerve repair device. Two different arrangements, rod-based and sheet-based designs, were tested within a clinically approved tube, NeuraWrap™, in a 5mm gap in the rat sciatic nerve (fig. 1). Cross sections were stained to detect neurofilament after 4 weeks *in vivo* and revealed where the axons were growing in relation to the EngNT structures (this was divided into three zones for the analysis, fig. 1). The axon density was significantly greater in zone 1 than in zone 3 in the devices ($P < 0.05$, one-way ANOVA). The rod-based arrangement (A) gave a higher axon density in zone 1, 3350 ± 143 axons/mm² (mean \pm SEM), compared to the sheet-based arrangement (B) (2920 ± 587 axons/mm²). The rod-based arrangement was more stable; there were no observed changes to its structure or orientation as a result of surgical handling or limb movement post-implantation. The designs are modular and can be adapted for the repair of bigger nerves by, for example, having multiple rod structures in the core of outer tubes or sheath wraps. Aligned cellular EngNT rods can form the basis of a functional conduit for peripheral nerve repair.

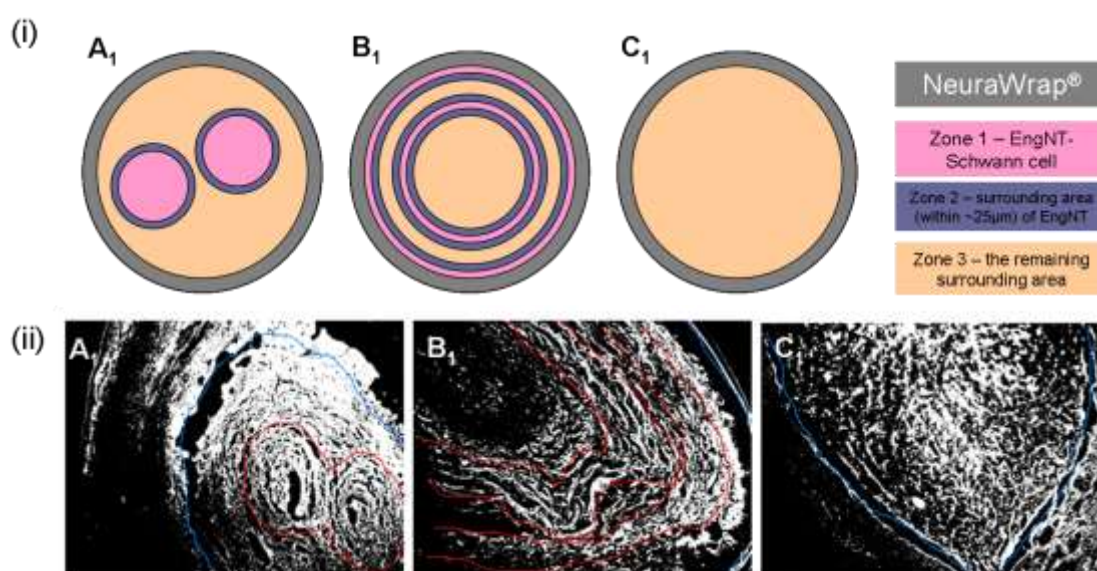


Figure 1 The different zones within a cross section of an EngNT device post-implantation.

(i) A key to show the different zones within the difference device designs: EngNT rods (A); EngNT sheets (B); and the empty NeuraWrap tube (C) after 4 weeks *in vivo* in a 5mm gap in rat sciatic nerve (not drawn to scale); (ii) are 10µm cross sections, as observed by auto fluorescence on a light microscope for the different device designs. The red outlines the EngNT material and the blue outlines the device core.